Amendment to the Specification:

Please amend the specification as follows:

Please replace the paragraph on page 1, lines 4 to 7, with the following amended paragraph:

The present application is a continuation-in-part of U.S. Serial No. 09/430,669, filed October 28, 1999, now issued U.S. Patent No. 6,329,187 ~~now pending~~; which is a divisional of U.S. Serial No. 09/066,544, filed April 24, 1998, now issued U.S. Patent 6,001,984; which is a continuation of U.S. Serial No. 08/651,572, filed May 22, 1996, now issued U.S. Patent 5,789,228, the contents of which are hereby incorporated by reference in their entirety.

Amendment to the Claims:

Please amend the claims as follows.

Please cancel claims 1 to 41 and 56 to 87, without prejudice.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

1 to 41. (canceled)

Claim 42 (original): A method of generating a nucleic acid encoding an endonuclease ~~variant~~ comprising:

obtaining a nucleic acid encoding an endonuclease comprising a sequence having at least about 50% sequence identity to a sequence as set forth in SEQ ID NO: 1, ~~sequences substantially identical thereto,~~ or sequences complementary thereto, ~~fragments comprising at least 30 consecutive nucleotides thereof, and fragments comprising at least 30 consecutive nucleotidesof the sequences complementary to SEQ ID NO: 1~~; and

modifying one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence.

Claim 43 (original): The method of claim 42, wherein the modifications are introduced by a method selected from the group consisting of error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, gene reassembly, gene site saturated mutagenesis and any combination thereof.

Claim 44 (original): The method of claim 42, wherein the modifications are introduced by error-prone PCR.

Claim 45 (original): The method of claim 42, wherein the modifications are introduced by shuffling.

Claim 46 (original): The method of claim 42, wherein the modifications are introduced by oligonucleotide-directed mutagenesis.

Claim 47 (original): The method of claim 42, wherein the modifications are introduced by assembly PCR.

Claim 48 (original): The method of claim 42, wherein the modifications are introduced by sexual PCR mutagenesis.

Claim 49 (original): The method of claim 42, wherein the modifications are introduced by *in vivo* mutagenesis.

Claim 50 (original): The method of claim 42, wherein the modifications are introduced by cassette mutagenesis.

Claim 51 (original): The method of claim 42, wherein the modifications are introduced by recursive ensemble mutagenesis.

Claim 52 (original): The method of claim 42, wherein the modifications are introduced by exponential ensemble mutagenesis.

Claim 53 (original): The method of claim 42, wherein the modifications are introduced by site-specific mutagenesis.

Claim 54 (original): The method of claim 42, wherein the modifications are introduced by gene reassembly.

Claim 55 (original): The method of claim 42, wherein the modifications are introduced by gene site saturated mutagenesis.

56 to 87 (canceled)

Claim 88 (currently amended): A method for modifying small molecules, comprising

providing ~~mixing~~ a polypeptide encoded by a polynucleotide comprising a sequence ~~as set forth in SEQ ID NO:1 and variants thereof,~~ having at least about 50% identity to SEQ ID NO:1 and encoding a polypeptide having an endoglucanase activity,

providing a small molecule; and

mixing the polypeptide with the [[a]] small molecule to produce a modified small molecule.

Claim 89 (original): The method of claim 88 wherein a library of modified small molecules is tested to determine if a modified small molecule is present within the library which exhibits a desired activity.

Claim 90 (original): The method of claim 89 wherein a specific biocatalytic reaction which produces the modified small molecule of desired activity is identified by systematically eliminating each of the biocatalytic reactions used to produce a portion of the library, and then testing the small molecules produced in the portion of the library for the presence or absence of the modified small molecule with the desired activity.

Claim 91 (original): The method of claim 90 wherein the specific biocatalytic reactions which produce the modified small molecule of desired activity is optionally repeated.

Claim 92 (original): The method of claim 90 or 91 wherein

the biocatalytic reactions are conducted with a group of biocatalysts that react with distinct structural moieties found within the structure of a small molecule,

each biocatalyst is specific for one structural moiety or a group of related structural moieties; and

each biocatalyst reacts with many different small molecules which contain the distinct structural moiety.

Claim 93 (new): A method of generating a nucleic acid encoding an endonuclease comprising:

obtaining a nucleic acid encoding an endonuclease, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 50% sequence identity to a sequence as set forth in SEQ ID NO: 1 or sequences complementary thereto; and

modifying one or more nucleotides in the sequence to another nucleotide, deleting one or more nucleotides in the sequence or adding one or more nucleotides to the sequence.

Claim 94 (new): A method of generating a nucleic acid encoding an endonuclease comprising:

obtaining a nucleic acid comprising a sequence as set forth in SEQ ID NO: 1 or sequences complementary thereto; and

modifying one or more nucleotides in the sequence to another nucleotide, deleting one or more nucleotides in the sequence or adding one or more nucleotides to the sequence.

Claim 95 (new): A method for modifying a small molecule comprising:

providing a polypeptide having an endoglucanase activity, wherein the polypeptide is encoded by a nucleic acid comprising at least 30 consecutive residue of a sequence having at least about 50% sequence identity to a sequence as set forth in SEQ ID NO:1 or sequences complementary thereto;

providing a small molecule; and

mixing the polypeptide with the small molecule to produce a modified small molecule.

Claim 96 (new): A method for modifying a small molecule comprising:

providing a polypeptide having an endoglucanase activity, wherein the polypeptide is encoded by a nucleic acid comprising a sequence as set forth in SEQ ID NO:1 or sequences complementary thereto;

providing a small molecule; and

mixing the polypeptide with the small molecule to produce a modified small molecule.

Claim 97 (new): The method of claim 93 or claim 95, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 55% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 98 (new): The method of claim 97, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 60% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 99 (new): The method of claim 98, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 65% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 100 (new): The method of claim 99, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 70% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 101 (new): The method of claim 100, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 75% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 102 (new): The method of claim 101, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 80% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 103 (new): The method of claim 102, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 85% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 104 (new): The method of claim 103, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 90% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 105 (new): The method of claim 104, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 95% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 106 (new): The method of claim 105, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 96% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 107 (new): The method of claim 106, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 97% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 108 (new): The method of claim 107, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 98% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 109 (new): The method of claim 108, wherein the nucleic acid comprises at least 30 consecutive residue of a sequence having at least about 99% sequence identity to a sequence as set forth in SEQ ID NO: 1.

Claim 110 (new): The method of claim 93 or claim 95, wherein the endonuclease activity comprises a carboxymethyl cellulase activity.

Claim 111 (new): A method of generating and identifying a nucleic acid encoding an endonuclease comprising:

obtaining a nucleic acid encoding an endonuclease comprising a sequence having at least about 50% sequence identity to a sequence as set forth in SEQ ID NO: 1 or sequences complementary thereto;

modifying one or more nucleotides in the sequence to another nucleotide, deleting one or more nucleotides in the sequence, or adding one or more nucleotides to the sequence; and

identifying a modified nucleic acid having an endonuclease activity.

Claim 112 (new): A method for modifying a small molecule such that the small molecule will have a desired activity comprising:

providing a polypeptide having an endoglucanase activity, wherein the polypeptide has at least about 50% sequence identity to a sequence as set forth in SEQ ID NO:1 or sequences complementary thereto;

providing a small molecule;

mixing the polypeptide with the small molecule to produce a modified small molecule; and,

testing the modified small molecule for the desired activity.

Claim 113 (new): A modified small molecule made by the method of claim 95 or claim 112.

Claim 114 (new): A nucleic acid made by the method of claim 93 or claim 111.

REMARKS

Status of the Claims

Pending claims

Claims 1 to 92 are pending.

Response to the Restriction Requirement

The instant application has been restricted to one of the following inventions under 35 U.S.C. §121:

Group I: Claims 1-23 and 67-85, drawn to an isolated nucleic acid molecule or fragment thereof useful as probes in hybridization.

Group II: Claims 24-39, 64, and 86-87, drawn to a purified polypeptide or variants thereof and an antibody which specifically binds to said purified polypeptide.

Group III: Claims 40-41, drawn to a method of producing a purified polypeptide which involves a host cell.

Group IV: Claims 42-55 and 88-92, drawn to a method of mutagenesis.

Group V: Claims 56-60, drawn to a computer readable medium having stored thereon a nucleic acid sequence or a polypeptide sequence.

Group VI: Claims 61-63, drawn to a method of comparing nucleic acid or polypeptide sequences and identifying differences therein as compared to reference nucleic acid or polypeptide sequences.

Group VII: Claim 65, drawn to a method of catalyzing the hydrolysis cellulose.

Group VIII: Claim 66, drawn to an assay for identifying functional polypeptide fragments or variant thereof.

Applicants elected Group IV, claims 42-55 and 88-92, drawn to a method of mutagenesis, with traverse

Claims canceled and added in the instant amendment

In the present response and amendment, claims 1 to 41 and 56 to 87, are canceled without prejudice; and new claims 93 to 114 are added. Thus, after entry of these amendments, claims 42 to 55 and 88 to 114 are pending and presented for consideration.

Outstanding Rejections

Claims 88 to 92 are rejected under 35 U.S.C. §112, first paragraph. Claims 42 to 55 and 88 to 92 are rejected under 35 U.S.C. §112, second paragraph. Claims 42 to 55 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Stemmer, U.S. Patent No. 6,277,638 (hereinafter "Stemmer"), in view of Knowles, et al., U.S. Patent No. 5,393,670 (hereinafter "Knowles"). Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to methods using a nucleic acid having at least about 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75%, 70%, 65%, 60%, 55%, or 50% sequence identity to an exemplary sequence of the invention can be found, inter alia, in the specification page 42, line 15, to page 43, line 2, and on page 56, lines 9 to 24. Support for claims directed to methods comprising identifying a nucleic acid modified by the method having an endonuclease activity can be found, inter alia, in the specification page 5, line 28 to page 6, line 5. Support for claims directed to methods comprising modifying a nucleic acid encoding an endonuclease, wherein the endonuclease activity comprises a carboxymethyl cellulase activity, can be found, inter alia, on page 3, lines 5 to 6.

Issues under 35 U.S.C. §112, first paragraph

Claims 88 to 92 are rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable these claims.

The Patent Office states that the specification is enabling for a method of modifying SEQ ID NO:1 and or close variants thereof which encode a particular polypeptide.

However, the Patent Office alleges that the specification is not enabling for a method of modifying, wherein the polypeptide to be modified is mixed with a small molecule to

produce a modified small molecule. It is alleged that because there is no guidance presented as regards how one is to produce a modified small molecule (to be mixed with an endonuclease of the invention), there is no showing as to how the method is to be accomplished.

Applicants respectfully note that in the method of claims 88 to 92, a polypeptide of the invention modifies a small molecule. The methods of claims 88 to 92 do not involve modifying a polypeptide of the invention (as is the case with claims 42 to 55).

Applicants respectfully aver that the specification sufficiently enabled the skilled artisan at the time of the invention to produce or make (or, e.g., purchase a library of) small molecules to be mixed with an endonuclease of the invention to practice the claimed methods, e.g., to make a modified small molecule. For example, the specification on page 70, line 21 to page 72, line 6, describes methods for modifying small molecules using a polypeptide (e.g., an endonuclease) of the invention. The specification states that any "starting compound," e.g., a small molecule, can be mixed with a polypeptide of the invention (see page 70, lines 21 to 28, of the specification):

> The present invention exploits the unique catalytic properties of enzymes. Whereas the use of biocatalysts (i.e., purified or crude enzymes, non-living or living cells) in chemical transformations normally requires the identification of a particular biocatalyst that reacts with a specific starting compound, the present invention uses selected biocatalysts and reaction conditions that are specific for functional groups that are present in many starting compounds, such as small molecules. Each biocatalyst is specific for one functional group, or several related functional groups, and can react with many starting compounds containing this functional group.

Any "starting compound," or small molecule, can be used in practicing the methods of the invention. One skilled in the art at the time of the invention, using the teaching of the specification, could have chosen any starting compound and practiced the method of the invention, including selecting a modified compound (e.g., small molecule) having a desired structure or activity without undue experimentation. As described by the specification, screening many alternative starting compounds, and products modified by the methods of the invention for a desired structure or activity, was a routine procedure at the time of the invention (see page 71, lines 16 to 21, of the specification):

Many of the procedural steps are performed using robotic automation enabling the execution of many thousands of biocatalytic reactions and screening assays per day as well as ensuring a high level of accuracy and reproducibility. As a result, a library of derivative compounds can be produced in a matter of weeks which would take years to produce using current chemical methods.

Additionally, the instant application has incorporated by reference PCT/US94/09174, published as WO 95/05475, that teaches many methods of modifying small molecules, see page 14, lines 8 to 13, which reads:

> Many of the procedural steps are performed using robotic automation enabling the execution of many thousands of biocatalytic reactions and screening assays per day as well as ensuring a high level of accuracy and reproducibility. As a result, a library of derivative compounds can be produced in a matter of weeks which would take years to produce using current chemical methods. (For further teachings on modification of molecules, including small molecules, see PCT/US94/09174, herein incorporated by reference in its entirety).

Accordingly, because the skilled artisan at the time of the invention could have practiced the claimed methods without undue experimentation, the rejection under 35 U.S.C. §112, first paragraph, can be withdrawn.

Issues under 35 U.S.C. §112, second paragraph

Claims 42 to 55 and 88 to 92 are rejected under 35 U.S.C. §112, second paragraph.

It is alleged that claim 42 is unclear. The instant amendment addresses this issue.

It is alleged that claim 88 is unclear. The instant amendment addresses this issue.

Issues under 35 U.S.C. §103

Claims 42 to 55 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Stemmer in view of Knowles.

The Patent Office states that Stemmer does not teach a nucleic acid as cited in claim 42, and that Knowles cures this defect in Stemmer by teaching a recombinant DNA encoding an endoglucanase comprising a sequence substantially identical to SEQ ID NO:1 of the instant invention.

However, Applicants respectfully aver that Knowles does not teach a nucleic acid comprising at least 30 consecutive residue of a sequence having at least about 50% sequence

identity to a sequence as set forth in SEQ ID NO: 1, or, a sequence having at least about 50% sequence identity to a sequence as set forth in SEQ ID NO: 1 (see amended claims 42 and 88, and new claims 93 to 96). Applicants have compared a scanned version of the nucleic acid sequence of Knowles to SEQ ID NO:1 using BIOEDIT™ (Tom Hall, Department of Microbiology, North Carolina State University). This BIOEDIT™ analysis shows that Knowles does not teach a nucleic acid used in the claimed methods. A BIOEDIT™ analysis of the amino acid sequences also shows that the sequence of Knowles does not have substantial sequence identity to the sequences used in the claimed methods. The results of Applicants' BIOEDIT™ analysis are attached as Exhibit A.

Accordingly, because Knowles does not cure the defect in Stemmer to teach the claimed methods of the instant invention, the rejection of 42 to 55 under 35 U.S.C. §103(a) as allegedly unpatentable over Stemmer in view of Knowles can be withdrawn.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs and 35 U.S.C. §103(a). Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present Response. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (858) 678-5070.

Respectfully submitted,

Date: July 23, 2003

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Exhibit A

Pairwise Alignment
Sequence 1: Fig.11A 5393670
Sequence 2: SEQIDNO1 09/888,224
Optimal Global aligment
Alignment score: -1036

Identities: 0.34

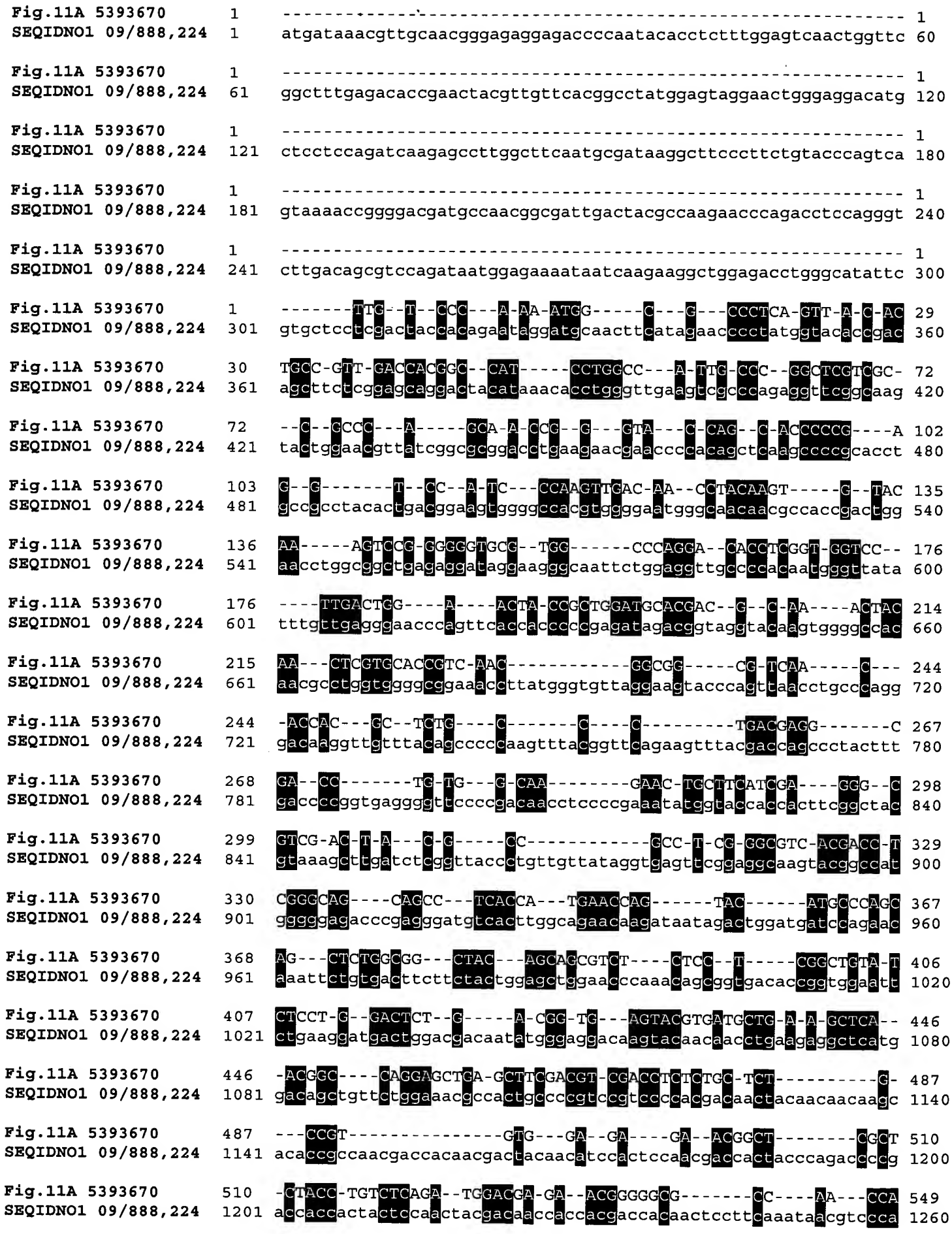
Fig.11A 5393670 1 ---------- 1
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Fig.11A 5393670 1 ---------- 1
SEQIDNO1 09/888,224 61 ggctttgagacaccgaactacgttgttcacggcctatggagtaggaactgggaggacatg 120
Fig.11A 5393670 1 ---------- 1
SEQIDNO1 09/888,224 121 ctcctccagatcaagagccttggcttcaatgcgataaggcttcccttctgtacccagtca 180
Fig.11A 5393670 1 ---------- 1
SEQIDNO1 09/888,224 181 gtaaaaccggggacgatgccaacggcgattgactacgccaagaacccagacctccagggt 240
Fig.11A 5393670 1 ---------- 1
SEQIDNO1 09/888,224 241 cttgacagcgtccagataatggagaaaataatcaagaaggctggagacctgggcatattc 300
Fig.11A 5393670 1 -------TTG--T--CCC---A-AA-ATGG-----C---G---CCCTCA-GTT-A-C-AC 29
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Fig.11A 5393670 30 TGCC-GTT-GACCACGGC--CAT-----CCTGGCC---A-TTG-CCC--GGCTCGTCGC- 72
SEQIDNO1 09/888,224 361 agcttctcggagcaggactacataaacacctgggttgaagtcgccagaggttcggcaag 420
Fig.11A 5393670 72 --C--GCCC---A-----GCA-A-CCG--G---GTA---C-CAG--C-ACCCCCG----A 102
SEQIDNO1 09/888,224 421 tactggaacgttatcggcgcggacctgaagaacgaacccacagctcaagccccgcacct 480
Fig.11A 5393670 103 G--G-------T--CC--A-TC---CCAAGTTGAC-AA--CCTACAAGT-----G--TAC 135
SEQIDNO1 09/888,224 481 gccgcctacactgacggaagtggggccacgtggggaatgggcaacaacgccaccgactgg 540
Fig.11A 5393670 136 AA-----AGTCCG-GGGGGTGCG--TGG------CCCAGGA--CACCTCGGT-GGTCC-- 176
SEQIDNO1 09/888,224 541 aacctggcggctgagaggatagggaagggcaattctggaggttgcccacaatgggttata 600
Fig.11A 5393670 176 ----TTGACTGG----A----ACTA-CCGCTGGATGCACGAC--G--C-AA----ACTAC 214
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Fig.11A 5393670 215 AA---CTCGTGCACCGTC-AAC-----------GGCGG-----CG-TCAA-----C--- 244
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Fig.11A 5393670 244 -ACCAC---GC--TCTG----C-------C----C---------TGACGAGG-------C 267
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Fig.11A 5393670 299 GTCG-AC-T-A---C-G-----CC-----------GCC-T-CG-GGCGTC-ACGACC-T 329
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Fig.11A 5393670 330 CGGGCAG----CAGCC---TCACCA---TGAACCAG------TAC------ATGCCCAGC 367
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Fig.11A 5393670 368 AG---CTCTGGCGG---CTAC---AGCAGCGTCT----CTCC--T-----CGGCTGTA-T 406
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Fig.11A 5393670 407 CTCCT-G--GACTCT--G-----A-CGG-TG---AGTACGTGATGCTG-A-A-GCTCA-- 446
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Fig.11A 5393670 446 -ACGGC----CAGGAGCTGA-GCTTCGACGT-CGACCTCTCTGC-TCT----------G- 487
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Fig.11A 5393670 487 ---CCGT---------------GTG---GA--GA----GA--ACGGCT--------CGCT 510
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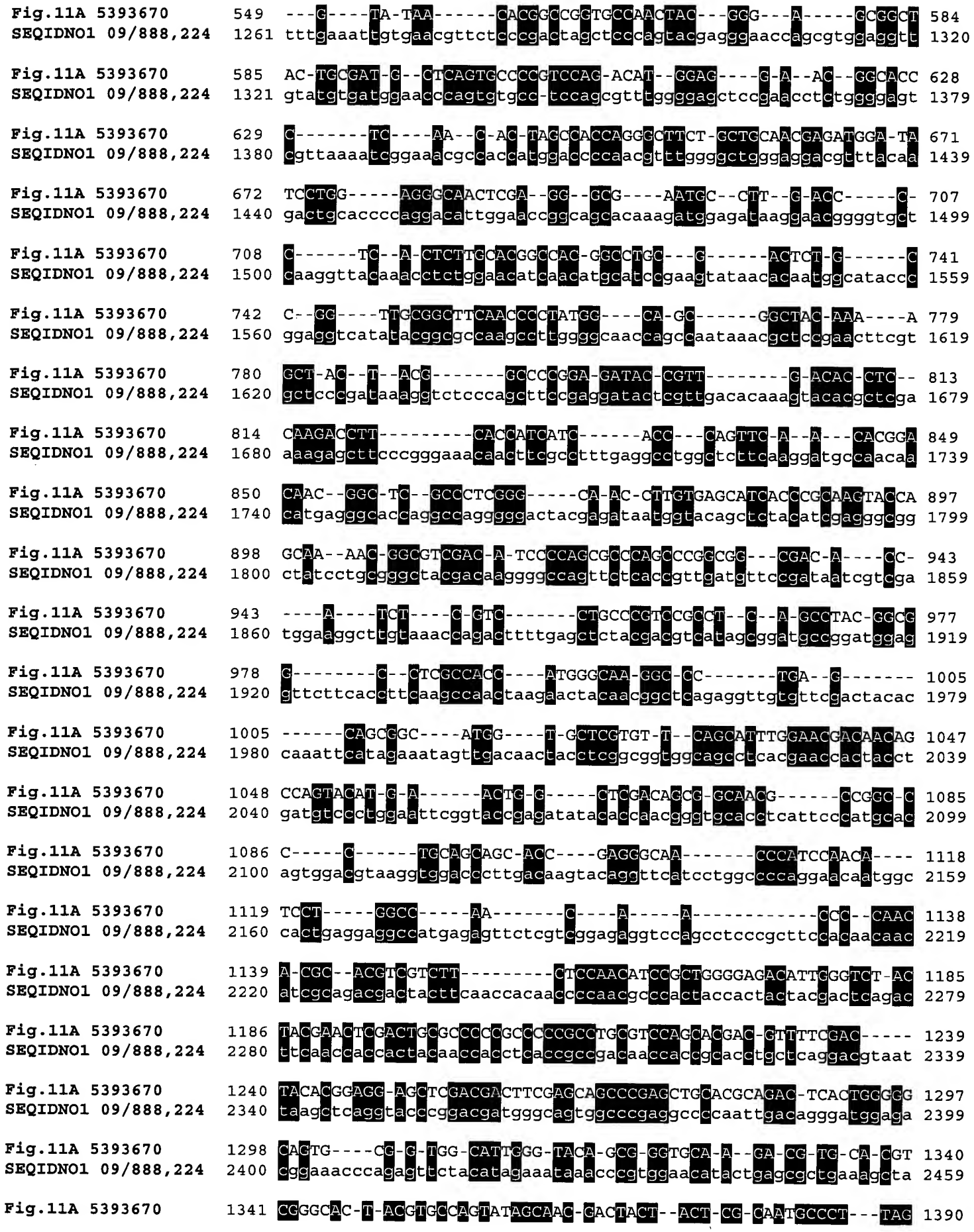
Fig.11A 5393670 549 ---G----TA-TAA------CACGGCCGGTGCCAACTAC---GGG---A-----GCGGCT 584
SEQIDNO1 09/888,224 1261 tttgaaattgtgaacgttctcccgactagctcccagtacgagggaaccagcgtggaggtt 1320
Fig.11A 5393670 585 AC-TGCGAT-G--CTCAGTGCCCCGTCCAG-ACAT--GGAG----G-A--AC--GGCACC 628
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Fig.11A 5393670 629 C-------TC----AA--C-AC-TAGCCACCAGGGCTTCT-GCTGCAACGAGATGGA-TA 671
SEQIDNO1 09/888,224 1380 cgttaaaatcggaaacgccaccatggacccaacgtttgggggctgggaggacgtttacaa 1439
Fig.11A 5393670 672 TCCTGG-----AGGGCAACTCGA--GG--GCG----AATGC--CTT--G-ACC-----C- 707
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Fig.11A 5393670 708 C------TC--A-CTCTTGCACGGCCAC-GGCCTGC---G------ACTCT-G------C 741
SEQIDNO1 09/888,224 1500 caaggttacaaacctctggaacatcaacatgcatccgaagtataacacaatggcataccc 1559
Fig.11A 5393670 742 C--GG----TTGCGGCTTCAACCCCTATGG----CA-GC------GGCTAC-AAA----A 779
SEQIDNO1 09/888,224 1560 ggaggtcatatacggcgccaagccttggggcaaccagccaataaacgctccggaacttcgt 1619
Fig.11A 5393670 780 GCT-AC--T--ACG-------GCCCCGGA-GATAC-CGTT--------G-ACAC-CTC-- 813
SEQIDNO1 09/888,224 1620 gctcccgataaaggtctcccagcttccgaggatactcgttgacacaaagtacacgctcga 1679
Fig.11A 5393670 814 CAAGACCTT---------CACCATCATC------ACC---CAGTTC-A--A---CACGGA 849
SEQIDNO1 09/888,224 1680 aaagagcttcccgggaaacaacttcgcctttgaggcctggctcttcaaggatgccaacaa 1739
Fig.11A 5393670 850 CAAC--GGC-TC--GCCCTCGGG-----CA-AC-CTTGTGAGCATCACCCGCAAGTACCA 897
SEQIDNO1 09/888,224 1740 catgagggcaccaggccaggggactacgagataatggtacagctctacatcgagggcgg 1799
Fig.11A 5393670 898 GCAA--AAC-GGCGTCGAC-A-TCCCCAGCGCCCAGCCCGGCGG---CGAC-A----CC- 943
SEQIDNO1 09/888,224 1800 ctatcctgcgggctacgacaaggggccagttctcaccgttgatgttccgataatcgtcga 1859
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Fig.11A 5393670 1005 ------CAGCGGC----ATGG----T-GCTCGTGT-T--CAGCATTTGGAACGACAACAG 1047
SEQIDNO1 09/888,224 1980 caaattcatagaaatagttgacaactacctcggcggtggcagcctcacgaaccactacct 2039
Fig.11A 5393670 1048 CCAGTACAT-G-A------ACTG-G-----CTCGACAGCG-GCAACG------CCGGC-C 1085
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Fig.11A 5393670 1119 TCCT-----GGCC-----AA-------C----A-----A----------CCC--CAAC 1138
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Fig.11A 5393670 1139 A-CGC--ACGTCGTCTT---------CTCCAACATCCGCTGGGGAGACATTGGGTCT-AC 1185
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Fig.11A 5393670 1186 TACGAACTCGACTGCGCCCCCGCCCCCGCCTGCGTCCAGCACGAC-GTTTTCGAC----- 1239
SEQIDNO1 09/888,224 2280 ttcaaccaccactacaaccacctcaccgccgacaaccacggcacgtgctcaggacgtaat 2339
Fig.11A 5393670 1240 TACACGGAGG-AGCTCGACGACTTCGAGCAGCCCGAGCTGCACGCAGAC-TCACTGGGGG 1297
SEQIDNO1 09/888,224 2340 taagctcaggtacccggacgatgggcagtggcccgaggcccccaattgacagggatggaga 2399
Fig.11A 5393670 1298 CAGTG----CG-G-TGG-CATTGGG-TACA-GCG-GGTGCA-A--GA-CG-TG-CA-CGT 1340
SEQIDNO1 09/888,224 2400 cggaaacccagagttctacatagaaataaacccgtggaacatactgagcgctgaaagcta 2459
Fig.11A 5393670 1341 CGGGCAC-T-ACGTGCCAGTATAGCAAC-GACTACT--ACT-CG-CAATGCCCT---TAG 1390

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SEQIDNO1 09/888,224   2460 cgccgagatgacctacaacttgagcagcggggttctccactacgtccaggccctggatag 2519

Fig.11A 5393670       1391 AGCGTTGACT 1400
SEQIDNO1 09/888,224   2520 tatatgatga 2529
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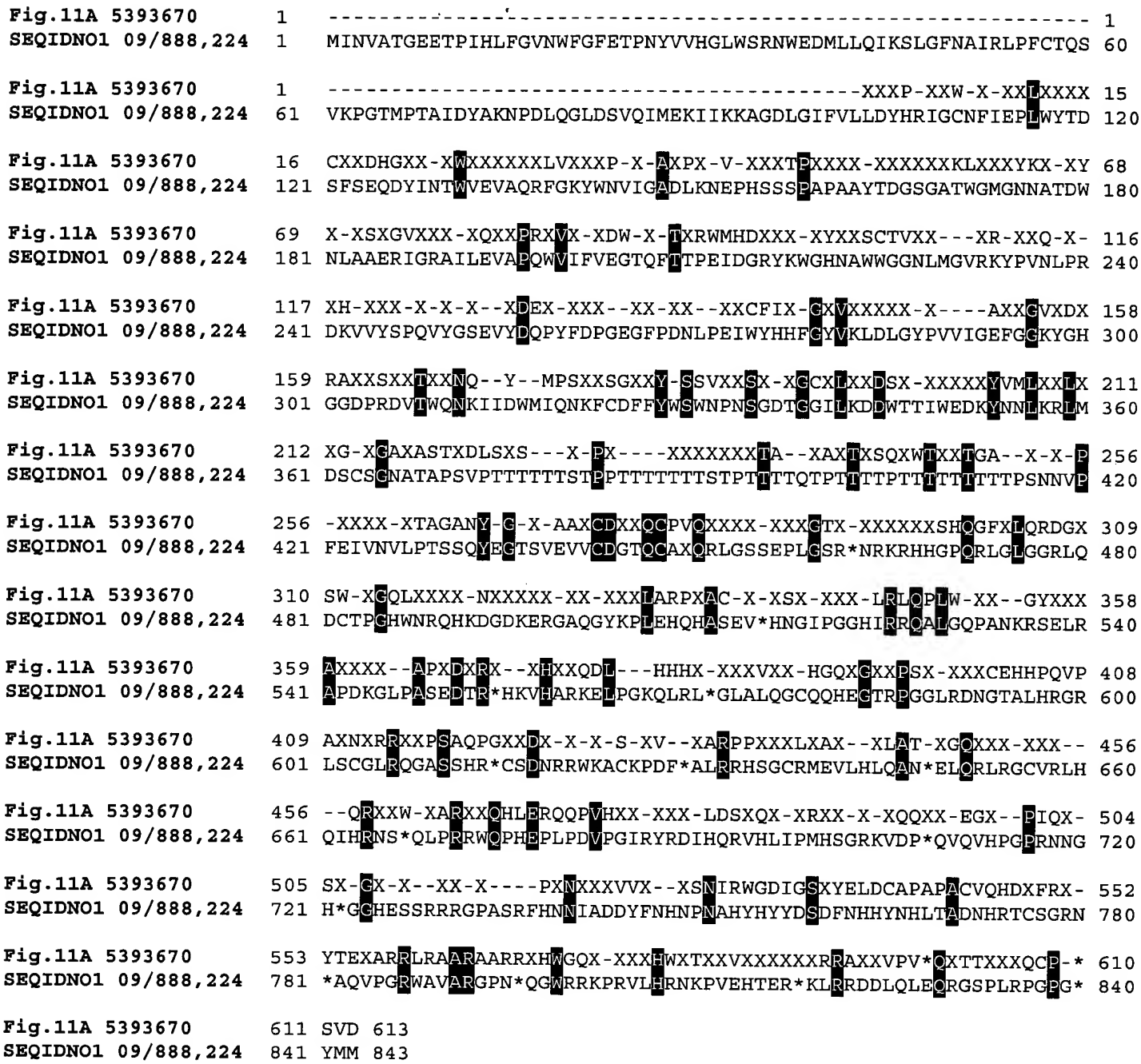
Fig.11A 5393670 1 ---------- 1
SEQIDNO1 09/888,224 1 MINVATGEETPIHLFGVNWFGFETPNYVVHGLWSRNWEDMLLQIKSLGFNAIRLPFCTQS 60
Fig.11A 5393670 1 ----------XXXP-XXW-X-XXLXXXX 15
SEQIDNO1 09/888,224 61 VKPGTMPTAIDYAKNPDLQGLDSVQIMEKIIKKAGDLGIFVLLDYHRIGCNFIEPLWYTD 120
Fig.11A 5393670 16 CXXDHGXX-XWXXXXXXLVXXXP-X-AXPX-V-XXXTPXXXX-XXXXXXKLXXXYKX-XY 68
SEQIDNO1 09/888,224 121 SFSEQDYINTWVEVAQRFGKYWNVIGADLKNEPHSSSPAPAAYTDGSGATWGMGNNATDW 180
Fig.11A 5393670 69 X-XSXGVXXX-XQXXPRXVX-XDW-X-TXRWMHDXXX-XYXXSCTVXX---XR-XXQ-X- 116
SEQIDNO1 09/888,224 181 NLAAERIGRAILEVAPQWVIFVEGTQFTTPEIDGRYKWGHNAWWGGNLMGVRKYPVNLPR 240
Fig.11A 5393670 117 XH-XXX-X-X-X--XDEX-XXX--XX-XX--XXCFIX-GXVXXXXX-X----AXXGVXDX 158
SEQIDNO1 09/888,224 241 DKVVYSPQVYGSEVYDQPYFDPGEGFPDNLPEIWYHHFGYVKLDLGYPVVIGEFGGKYGH 300
Fig.11A 5393670 159 RAXXSXXTXXNQ--Y--MPSXXSGXXY-SSVXXSX-XGCXLXXDSX-XXXXXYVMLXXLX 211
SEQIDNO1 09/888,224 301 GGDPRDVTWQNKIIDWMIQNKFCDFFYWSWNPNSGDTGGILKDDWTTIWEDKYNNLKRLM 360
Fig.11A 5393670 212 XG-XGAXASTXDLSXS---X-PX----XXXXXXXTA--XAXTXSQXWTXXTGA--X-X-P 256
SEQIDNO1 09/888,224 361 DSCSGNATAPSVPTTTTTTSTPPTTTTTTTSTPTTTTQTPTTTPTTTTTTTTPSNNVP 420
Fig.11A 5393670 256 -XXXX-XTAGANY-G-X-AAXCDXXQCPVQXXXX-XXXGTX-XXXXXXSHQGFXLQRDGX 309
SEQIDNO1 09/888,224 421 FEIVNVLPTSSQYEGTSVEVVCDGTQCAXQRLGSSEPLGSR*NRKRHHGPQRLGLGGRLQ 480
Fig.11A 5393670 310 SW-XGQLXXXX-NXXXXX-XX-XXXLARPXAC-X-XSX-XXX-LRLQPLW-XX--GYXXX 358
SEQIDNO1 09/888,224 481 DCTPGHWNRQHKDGDKERGAQGYKPLEHQHASEV*HNGIPGGHIRRQALGQPANKRSELR 540
Fig.11A 5393670 359 AXXXX--APXDXRX--XHXXQDL---HHHX-XXXVXX-HGQXGXXPSX-XXXCEHHPQVP 408
SEQIDNO1 09/888,224 541 APDKGLPASEDTR*HKVHARKELPGKQLRL*GLALQGCQQHEGTRPGGLRDNGTALHRGR 600
Fig.11A 5393670 409 AXNXRRXXPSAQPGXXDX-X-X-S-XV--XARPPXXXLXAX--XLAT-XGQXXX-XXX-- 456
SEQIDNO1 09/888,224 601 LSCGLRQGASSHR*CSDNRRWKACKPDF*ALRRHSGCRMEVLHLQAN*ELQRLRGCVRLH 660
Fig.11A 5393670 456 --QRXXW-XARXXQHLERQQPVHXX-XXX-LDSXQX-XRXX-X-XQQXX-EGX--PIQX- 504
SEQIDNO1 09/888,224 661 QIHRNS*QLPRRWQPHEPLPDVPGIRYRDIHQRVHLIPMHSGRKVDP*QVQVHPGPRNNG 720
Fig.11A 5393670 505 SX-GX-X--XX-X----PXNXXXVVX--XSNIRWGDIGSXYELDCAPAPACVQHDXFRX- 552
SEQIDNO1 09/888,224 721 H*GGHESSRRRGPASRFHNNIADDYFNHNPNAHYHYYDSDFNHHYNHLTADNHRTCSGRN 780
Fig.11A 5393670 553 YTEXARRLRAARAARRXHWGQX-XXXHWXTXXVXXXXXXRRAXXVPV*QXTTXXXQCP-* 610
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Fig.11A 5393670 611 SVD 613
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